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EXAMINER	
LOCKARD, JON MCCLELLAND	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,679	PLOUET ET AL.	
	Examiner	Art Unit	
	JON M. LOCKARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18* is/are pending in the application.

4a) Of the above claim(s) *12 and 15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11,13,14 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *10-18* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 February 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/1/06, 10/19/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 10-14 and 18, in so far as they are drawn to a method treatment comprising administering a polypeptide, in the reply filed on 30 January 2008 is acknowledged. Applicant's election with traverse of SEQ ID NO:12 in the reply is also acknowledged. The traversal is on the ground(s) that the cited patent fails to teach or such the claimed methods and therefore cannot be used to establish the claims lack a corresponding special technical feature. This is not found persuasive because, while the Examiner agrees that U.S. Patent No. 5,780,263 does not anticipate or render obvious the claimed methods, the inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Pursuant to 37 C.F.R. § 1.475(B-D), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto (i.e., method of making or method of using). Accordingly, the main invention (Group I) comprises the first recited method, a method of treatment comprising administering a polypeptide. Groups II-VI do not share the same or corresponding special technical feature because the Group II invention is drawn to a method of treatment comprising administering a polynucleotide, Group III is drawn to a method of treatment comprising administering an antibody, Group IV is drawn to polypeptides and pharmaceutical compositions comprising the same, Group V is drawn to polynucleotides and compositions

comprising the same, and the Group VI invention is drawn to antibodies and pharmaceutical compositions comprising the same. Lack of unity is shown because these inventions lack a common utility which is based upon a common technical feature which has been identified as the basis for that common utility. With regard to the restriction requirement between the individual polypeptides, antibodies, and polynucleotides, Applicant argues that even if the polypeptide are different in their structure, their common feature resides in their common inhibiting activity, and all the polynucleotides are derived from the same gene corresponding to SEQ ID NO:1 and thus have the same chromosomal location. This is not found persuasive because in order for unity of invention to exist for the individual polypeptides, for example, there needs to exist a common function as well as a common structure that is essential to that function. In the instant case, lack of unity is shown because these compounds and methods of using them lack a common utility which is based upon a common structural feature which has been identified as the basis for that common utility.

2. The requirement is still deemed proper and is therefore made FINAL.

3. Claims 12 and 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 30 January 2008.

Status of Application, Amendments, and/or Claims

4. The response filed 30 January 2008 has been received and entered in full. Claims 10 and 18 have been amended, and claims 12 and 15-17 have been withdrawn as discussed above.

Therefore, claims 10-18 are pending, and claims 10-11, 13-14, and 18 are the subject of this Office action. It is noted that the elected invention is SEQ ID NO:12, and the claims have been examined to the extent that they read on such.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on 01 February 2006 and 19 October 2006 have been considered by the examiner.

Drawings

6. Figures 1-5 are objected to because they are too dark for the Examiner to reasonably interpret.

7. Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should *not* be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in

the next Office action. The objection to the drawings will not be held in abeyance.

Specification

8. The disclosure is objected to because of the following informalities:

9. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant is requested to avoid the use of "novel" in the title, as patents are presumed to be novel and unobvious. Appropriate correction is suggested.

Claim Objections

10. Claims 10-11, 13-14, and 18 are objected to because of the following informalities. Claims 10-11, 13-14, and 18 encompass non-elected inventions, e.g., proteins of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, and SEQ ID NO:10; polynucleotides of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, and SEQ ID NO;11; and anti-idiotypic antibody of the NOV protein. Appropriate correction is suggested.

Claim Rejections - 35 USC § 112, 1st Paragraph (Enablement)

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 10-11, 13-14 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of (1) treating cancer and (2) inhibiting endothelial cell proliferation or activation in a subject, comprising administering to a person in need of said inhibition a pharmaceutically effective amount of a protein, wherein the protein consists of the amino acid sequence SEQ ID NO:12, does not reasonably provide enablement for (1) a method for treating any and all pathologies requiring the inhibition or activation of endothelial cells, or (2) a method for treating any and all pathologies requiring the inhibition or activation of endothelial cells, including cancer, comprising administering to a person in need of said inhibition a pharmaceutically effective amount of a protein, wherein the protein is represented by the sequence of SEQ ID NO:12, a sequence derived from SEQ ID NO:12, in particular by substitution, deletion or addition of one or more amino acids, or any sequence homologous to SEQ ID NO:12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

13. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

14. The claims are drawn quite broadly to a method for the treatment: of pathologies

requiring the inhibition of endothelial proliferation, in particular within the framework of the following pathologies: age-related macular degeneration, diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular Castelman's disease and Kaposi's sarcoma, or of pathologies requiring the inhibition of endothelial activation, in particular within the framework of the following pathologies: allograft and xenograft rejection, acrocyanosis, scleroderma, or within the framework of the preparation of grafts between collection and transplantation, said method comprising the administration of a pharmaceutically acceptable amount: of a protein characterized in that it comprises or is constituted by a sequence represented by SEQ ID NO:12 or a sequence derived from SEQ ID NO:12, in particular by substitution, deletion or addition of one or more amino acids, as well as any sequence homologous to SEQ ID NO:12, providing that this derived sequence exhibits an angiogenesis-inhibiting activity. The claims also recite wherein the pathology in cancer.

15. The specification teaches that the Nov protein (SEQ ID NO:2) binds VEGF165 (Fig 1 and 2; pg 17). The specification also teaches the following regarding the protein of SEQ ID NO:12 (the C-terminal fragment of the Nov protein consisting of amino acid residues 188-357 of SEQ ID NO:2): inhibits the migration of human umbilical artery endothelial cells (HUAEC) in the presence (Fig. 6A) and absence (Fig. 6B) of stimulation with $VEGF_{165}$ (See pg 22); inhibits the proliferation of HUAECs in response to stimulation with $VEGF_{165}$ (Fig. 7A) and bFGF (Fig. 7B) (See pg 22-23); and inhibits LPS-induced corneal angiogenesis (Fig. 8B; pg 23). While the Specification provides adequate direction and guidance on how to make and use the polypeptide of SEQ ID NO:12 in a method of (1) treating cancer and (2) inhibiting endothelial cell proliferation or activation in a subject, comprising administering to a person in need of said

inhibition a pharmaceutically effective amount of a protein, wherein the protein consists of the amino acid sequence SEQ ID NO:12, the specification fails to describe variants or derivatives of SEQ ID NO:12 that also inhibit endothelial cell proliferation or activation, or that inhibit angiogenesis, and it would require undue experimentation to determine such. Other than the polypeptide of SEQ ID NO:12, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (1) which portions of the protein of SEQ ID NO:12 are critical to the angiogenesis-inhibiting activity of the protein of SEQ ID NO:12; and (2) what modifications e.g., substitutions, deletions, or additions) one can make to SEQ ID NO:12 that will result in protein mutants or variants with the same function/activity as the protein of SEQ ID NO:12. The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and unpredictable, and that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions.

16. The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various

sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions, and modifications), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, that may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2).

17. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function; and the breadth of the claims which fail to

recite any structural, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

18. The specification teaches that the Nov protein (SEQ ID NO:2) binds VEGF165 (Fig 1 and 2; pg 17). The specification also teaches the following regarding the protein of SEQ ID NO:12 (the C-terminal fragment of the Nov protein consisting of amino acid residues 188-357 of SEQ ID NO:2): inhibits the migration of human umbilical artery endothelial cells (HUAEC) in the presence (Fig. 6A) and absence (Fig. 6B) of stimulation with $VEGF_{165}$ (See pg 22); inhibits the proliferation of HUAECs in response to stimulation with $VEGF_{165}$ (Fig. 7A) and bFGF (Fig. 7B) (See pg 22-23); and inhibits LPS-induced corneal angiogenesis (Fig. 8B; pg 23). While the Specification provides adequate direction and guidance on how to make and use the polypeptide of SEQ ID NO:12 in a method of (1) treating cancer and (2) inhibiting endothelial cell proliferation or activation in a subject, comprising administering to a person in need of said inhibition a pharmaceutically effective amount of a protein, wherein the protein consists of the amino acid sequence SEQ ID NO:12, there is no guidance on how to treat every pathology requiring the inhibition of endothelial proliferation or activation. One skilled in the art would not know, with any level of predictability, that the administration of an undetermined amount of the protein of SEQ ID NO:12 would lead to the treatment pf every possible pathology requiring the inhibition of endothelial proliferation or activation.

19. The instant specification does not teach how to treat every possible pathology requiring the inhibition of endothelial proliferation or activation. The specification fails to disclose how to

assess *in vivo* a pharmaceutically effective amount of the protein of SEQ ID NO:12 for the treatment of every possible pathology requiring the inhibition of endothelial proliferation or activation. The art teaches that the goal of delivering proteins and peptides noninvasively has only achieved modest success, with poor applicability to proteins and peptides (See for example Pettit et al. "The development of site-specific drug-delivery systems for protein and peptide biopharmaceuticals". Trends Biotechnol. 16: 343-349, 1998; See especially pg 343, col 1-2). The problems posed by proteins and peptides are their large molecular size, electrical charge, relatively hydrophilic nature, and relative instability in environments of extreme pH or proteolytic activity (such as the stomach and intestine) (pg 343, col 2). Pettit et al. review several routes of protein administration and the limitations that have been encountered. For example, limited success has been achieved delivering proteins and peptides orally because of: 1) poor intrinsic permeability across intestinal epithelium, 2) susceptibility to enzymatic attack, 3) rapid post-absorptive clearance, and 4) chemical instability (pg 344-345). Although much effort has been given to the transdermal delivery of pharmaceutical products, clinical applications have been limited to non-protein drugs because of the skin's poor permeability to proteins and peptides (pg 343, col 2). Additionally, proteins or peptides administered systemically must resist clearance via molecular filtration by the kidney and clearance by the reticuloendothelial system (pg 345, col 2). Therefore, the state of the prior art establishes the unpredictability of delivering proteins to a subject. In the absence of this guidance, a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of the protein of SEQ ID NO:12, and making a determination of whether a successful result was achieved. The instant situation is directly analogous to that which was

addresses in *In re Colianni*, 195 USPQ 150, (CCPA 1977), which held that:

> "a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

20. The only working example presented in the instant specification that describe the inhibition of angiogenesis in vivo is the inhibition of LPS-induced corneal angiogenesis, and thus does not disclose treatment of conditions commensurate in scope with the claims.

21. Thus, in view of the lack of teachings and unpredictability of the art set forth above and the lack of working examples, the instant specification is not found to be enabling for a method for treating every pathology requiring the inhibition of endothelial proliferation or activation. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use the Applicants' invention as currently claimed.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

22. Claims 10-11, 13-14, and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

23. The claims are drawn quite broadly to a method for the treatment: of pathologies requiring the inhibition of endothelial proliferation, in particular within the framework of the following pathologies: age-related macular degeneration, diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular Castelman's disease and Kaposi's sarcoma, or of pathologies requiring the inhibition of endothelial activation, in particular within the framework of the following pathologies: allograft and xenograft rejection, acrocyanosis, scleroderma, or within the framework of the preparation of grafts between collection and transplantation, said method comprising the administration of a pharmaceutically acceptable amount: of a protein characterized in that it comprises or is constituted by a sequence represented by SEQ ID NO:12 or a sequence derived from SEQ ID NO:12, in particular by substitution, deletion or addition of one or more amino acids, as well as any sequence homologous to SEQ ID NO:12, providing that this derived sequence exhibits an angiogenesis-inhibiting activity. The claims also recite wherein the pathology in cancer. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of the recitation “constituted by a sequence represented by SEQ ID NO:12 or a sequence derived from SEQ ID NO:12, in particular by substitution, deletion or addition of one or more amino acids" and a desired functional property in the form of the recitation of “exhibits an angiogenesis-inhibiting activity”. However, there is no identification of any particular portion of the structure

that must be conserved. While the specification provides adequate written description for a polypeptide consisting of the amino acid sequence SEQ ID NO:12 that inhibits angiogenesis, it does not provide adequate written description for a commensurate number of the claimed species of variants and derivatives of SEQ ID NO:12 that also inhibit angiogenesis. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is the polypeptide consisting of the amino acid sequence SEQ ID NO:12, and the description of one species of polypeptide (SEQ ID NO:12) is not adequate written description of an entire genus of functionally equivalent polypeptides, which incorporate all variants and derivatives encompassed by the claims.

24. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

25. With the exception of the polypeptide of SEQ ID NO:12 referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed antagonists, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The product itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

26. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

27. Therefore, only the polypeptide consisting of the amino acid sequence SEQ ID NO:12, but not the full breadth of the claims, meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112

28. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

29. Claims 10-11, 13-14, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

30. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim

indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 10 and 18 recite the broad recitation "in particular within the framework of the following pathologies: age-related macular degeneration, diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas", and the claim also recites "in particular Castelman's disease and Kaposi's sarcoma" which is the narrower statement of the range/limitation.

31. Claims 10-11, 13-14, and 18 are rejected as indefinite for reciting the phrase "represented by". Without knowing whether the limitation refers to a protein consisting of the amino acid sequence of SEQ ID NO:12, a protein corresponding to SEQ ID NO:12, or a protein typified by SEQ ID NO:12 (and to what degree, structurally and/or functionally), the metes and bounds of the claim cannot be determined. It is noted that for purposes of examination, the Examiner has interpreted the claims as reading on variants, derivatives, homologs, and orthologs of SEQ ID NO:12.

32. Regarding claims 10-11, 13-14, and 18, the phrase "in particular" renders the claims indefinite because it is unclear whether the limitations following the phrase are intended to limit the scope of the claims. See MPEP § 2173.05(d). It is noted that for purposes of examination, the Examiner has interpreted the phrase as being exemplary rather than limiting.

33. Claims 10-11, 13-14, and 18 are rejected as being indefinite because it is unclear what is meant by the phrase "having homology of at least approximately". Without knowing whether

the phrase requires homology over the entire length of the molecule or just a portion, or if there is a lower limit of to the percent homology or if it is variable, the metes and bounds of the claims cannot be determined.

Summary

34. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao, Ph.D.**, can be reached on **(571) 272-0939**. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jon M. Lockard, Ph.D.
May 27, 2008

/Jon M Lockard/
Examiner, Art Unit 1647